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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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08/311,489 09/23/94 WANG

EXAMINER 149

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18M1/1002

EISENSCHENK, F.
ART UNIT PAPER NUMBER

9

DATE MAILED: 1816

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

10/02/96

☒ This application has been examined ☒ Responsive to communication filed on 6/20/96 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

- | | |
|-------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| 1. <input type="checkbox"/> Notice of References Cited by Examiner, PTO-892. | 2. <input type="checkbox"/> Notice of Draftsman's Patent Drawing Review, PTO-948. |
| 3. <input type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449. | 4. <input type="checkbox"/> Notice of Informal Patent Application, PTO-152. |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input type="checkbox"/> |

Part II SUMMARY OF ACTION

1. ☒ Claims 1-14 are pending in the application.
Of the above, claims are withdrawn from consideration.
2. ☒ Claims 15-16 have been cancelled.
3. ☐ Claims are allowed.
4. ☒ Claims 1-14 are rejected.
5. ☐ Claims are objected to.
6. ☐ Claims are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. ; filed on
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

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EXAMINER'S ACTION

15. Applicants' comments regarding the drawing requirements is noted. Formal drawings will be required upon the identification of allowable subject matter.
16. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

17. Claims 1-14 are rejected under 35 U.S.C. § 103 as being unpatentable over Sindelar et al. ('499) in view of Auda et al. (Rheumatol. Int.), Wurtzer et al. (Complement Inflamm.), and Montz et al. (Cell. Immunol.). Claims 1-14 are drawn to methods for the treatment of established joint inflammation comprising the administration of an effective amount of a C5 blocker which does not block the functions of early complement components and further comprising the determination of the C5a and/or C5b level through ELISA assays or chemotactic assays to evaluate the patient's response to the treatment protocol. The patent teaches methods for the treatment of established joint inflammation comprising the administration of an effective amount of a C5 blocker. The invention of '499 is taught to be useful in the treatment of inflammatory disorders, such as rheumatoid arthritis, through the selective inhibition of C5 (see Table 3, claims 3-13, columns 5-10, and columns 22-23). Rheumatoid arthritis is considered an established joint inflammation, i.e. an inflammatory disease (see specification, page 11). By inhibiting the cleavage of C5, the inhibitors of '499 substantially inhibit the cell-lysing ability of complement in the serum of a patient as well as chemotactic attraction of cells involved in the inflammatory response (see

Montz et al.). The method of the '499 patent would also substantially reduce the level of C5b-9 in the plasma of a patient because the compounds of the '499 patent inhibit the cleavage and activation of C5 into C5a and C5b. According to Figures 2-3 of the '499 patent, the compounds of the patent are capable of reducing the cell lysing ability of complement by at least 10% as well as the amount of C5a by at least 10%. The blockers of the '499 patent also do not appear to substantially interfere with the cleavage of C3 (see Figure 2). The reference differs from the claimed invention in that a C5 inhibitor which did not effect the early C components is not taught. Wurznier et al. and Montz et al. teach C5 inhibitors which do not effect the early C components. These C5 inhibitors are C5 specific antibodies. By blocking C5 activation, one of ordinary skill in the art would have recognized that the chemotactic effects of C5 would be blocked as would the ability of the molecule to stimulate the oxidative burst in monocytes and neutrophils. Such chemotaxis and oxidative burst is associated with tissue injury in inflammatory joint disease (see Sindelar, columns 4-6). Therefore, one skilled in the art would have been motivated to treat inflammatory joint diseases with compounds capable of specifically disrupting the inflammatory response, such as C5 inhibitors). Auda et al. teach the measurement of complement activation products in patients suffering chronic rheumatic diseases and that such measurements provide additional information which allows for the prediction of patient clinical status (see Discussion). Auda further teach that the monitoring of C5b-9 levels in patients may provide for a more sensitive indicator of patient status than other indicators of disease status (Discussion, page 188, last 2 paragraphs). Such an assay would allow for the measurement of C5b levels within the C5b-9 complexes. Wurznier teaches the inhibition of terminal C components by monoclonal antibodies which are specific for C5 (see Abstract and Discussion). Wurznier teaches the production of specific tools (i.e., antibodies) which influence the formation of MAC and the activation of C5.

One of ordinary skill in the art at the time the invention was made would have been motivated to use the teachings of Sindelar et al. with the teachings of Auda

et al., Montz et al., and Wurzner et al. to arrive at a method of inhibiting inflammatory joint disease through the administration of C5 inhibitory antibodies and to determine the levels of C5a and/or C5b in the fluid samples of patients being treated according to the teachings of Sindelar in order to determine the clinical status of the patients so treated. One of ordinary skill in the art would have recognized that inhibitory antibodies were analogous to the compounds taught in Sindelar for the inhibition of C5 activation and that such inhibition of C5 would have reduced the inflammatory response by reducing infiltration of PML. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants' traversal of the previous rejection made under 35 USC 103 is noted. In view of the new grounds of rejection, necessitated by the amendment to the claims, it is considered moot. However, as the arguments relate to the present rejection, they will be addressed. It appears that Applicant argues that the Sindelar patent is not enabled, stating that "Surely, workers of ordinary skill in the art did not reasonably expect that these compounds would successfully treat all of the listed disease conditions." This argument is noted, however Applicant is reminded that the claims of all issued patents bear a presumption of validity, i.e. enablement, novelty, and non-obviousness. See 35 U.S.C. §282. In this case, the claims of Sindelar bear a presumption of validity with respect to the treatment of patients having undesirable or inappropriate complement activity (i.e. patients suffering from rheumatoid arthritis, such patients being art recognized to have abnormal levels of complement activation products, see Auda et al., entire document, especially Results). The declaration filed has also been considered but not found persuasive in view of Auda et al. which clearly indicates the involvement of complement in rheumatoid arthritis and the recruitment of PML. This teaching would have led one of ordinary skill in the art to recognize that inflammatory joint disease would have been treated through the inhibition of complement activation and prevention of C5 activation (to prevent the initiation of C5a mediated chemotaxis of cells).

18. No claim is allowed. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. § 706.07(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

This application may be subject to the provisions of Public Law 103-465, effective June 8, 1995. Accordingly, if this application has been pending for at least two years as of June 8, 1995, taking into account any reference to an earlier filed application under 35 U.S.C. 120, 121 or 365(c), applicant, under 37 CFR 1.129(a), is entitled to have a first submission entered and considered on the merits if, prior to abandonment, the submission and the fee set forth in 37 CFR 1.17(r) are filed prior to the filing of an appeal brief under 37 CFR 1.192.

THIS APPLICATION IS NOT SUBJECT TO PUBLIC LAW 103-465.

19. Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). THE CM1 FAX CENTER TELEPHONE NUMBER IS (703) 308-4242
20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher Eisenschenk whose telephone number is (703) 308-0452. The examiner can normally be reached Monday through Thursday from 6:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 180 receptionist whose telephone number is (703) 308-0196.

October 1, 1996
Christopher Eisenschenk, Ph.D.
Primary Examiner
Group 1800

